REMARKS

Claims 25, 57, 59 and 66 are currently amended. Claims 50 and 65 are canceled. New claim 67 is added. Reconsideration of the Application is requested in light of the amendments above and remarks below.

I: Claim Objections

Claims 25 and 59 were objected to for containing parenthesis. While Applicants are not aware of any rule(s) that prohibits the use of a parenthetical in a claim, Claims 25 and 59 are currently amended to remove the parenthetical, accordingly the objection is moot. Reconsideration is urged.

Claims 59-66 were objected to as being substantial duplicates of claims 25-30, 50 and 57. Applicants traverse this objection. The Examiner has stated that "it is proper after allowing one claim to object to the other as being a substantial duplicate of the allowed claim". Applicants note that claims 25-30, 50, 57 and 59-66 are currently rejected. No claim has been allowed by the Examiner. Thus, even assuming that the rejection is proper (which Applicants do not concede is proper), the objection is not ripe. For example, the varying claim terms could be included, if necessary, in an Appeal. Reconsideration of the Objection is urged.

II: The Rejection of Claims 29 and 63 Under 35 U.S.C. § 112, first paragraph (Written Description)

Claims 29 and 63 stand rejected under 35 U.S.C. 112 as allegedly lacking written description support. The Examiner contends that "while there is support in the specification for each of said substitutions (original claims 1 and 2, specification at page 12, lines 28-33 and page 13, lines 14-19), the examiner is unable to locate adequate support in the specification for the combination of said three mutations. There is no indication that the triple substitution comprising R118K, R320K and R459K was within the scope of the invention . . ." Applicants traverse this rejection.

The written description requirement of the Patent Code is fulfilled when the patent specification describes the claimed invention in sufficient detail such that one skilled in the art can reasonably conclude that the inventor had possession of the claimed invention. *See Vas-Cath, Inc. v. Mahurkar*, 19 USPQ2d 1111, 1116 (Fed. Cir. 1991). The written description as filed is presumed to be adequate, unless or until sufficient evidence or reasoning to the contrary has been presented by the examiner to rebut the presumption. *See In re Marzocchi*, 169 USPQ 367 (CCPA 1971).

Under this standard, the Examiner's conclusion that the specification only provides adequate written description support for each of the substitutions is plainly incorrect. The specification discloses, and one skilled in the art would clearly recognize, that the scope of the present invention includes one or more of the substitutions in original claims 1 and 2. For example, original claim 1 refers to variants which include an alteration "at **one or more** of the following positions:
R28, **R118**, N174; R181, G182, D183, G184, G186, W189, N195, M202, Y298, N299, K302, S303, N306, R310, N314; **R320**, H324, E345, Y396, R400, W439, R444, N445, K446, Q449, **R458**, N471, and N484.. ." See Original claim 1, where the alterations are listed in an alternative format (Bold added for emphasis).

Original claim 2 clearly describes, the variant of claim 1, which further "comprises **one or more** of the following mutations: Delta G184; Delta (R181-G182); Delta (D183-G184); R28N,K; S94K; **R118K**; N125A,R,K; N174D; R181Q,E,K; G186R; W189R,K; N195F; M202L; Y298H,F; N299A; K302R, S303Q, N306G,D,R,K; R310A,K,Q,E,H,D,N; N314D; **R320K**; H324K; E345R,D,K,N; Y396F; R400T,K; W439R; R444K; N445K,Q; K446N; Q449E; **R458K**; N471E; N484Q. . ." *See* Original Claim 2 (Bold added for emphasis).

Moreover, the Examiner has also correctly cited portions of the specification which provide support for these original claims. As Applicants included the terms "one or more", selections from these groupings, including but not limited to triple selections, are clearly envisioned by an artisan once apprised of Applicants' invention. Accordingly, an artisan would reasonably conclude that Applicants were not only in possession of single substitutions at positions 118, 320 and 458, but also that Applicants had possession of triple substitution as specified by the claims. Indeed, based on the high level of skill in the art, the alternative claim language of original claims 1 and 2 conveys to the artisan that Applicants were in possession of the claimed invention.

Notwithstanding the above, the Examiner has not provided sufficient evidence or reasoning to rebut that the specification provides an adequate written description for the triple substitutions claimed. In this regard, the Examiner contends that a number of additional representative species are required to be disclosed in the specification. Applicants note that numerous variant embodiments include, *inter alia*, triple substitutions, and are shown on pages 16-19.

Therefore, Applicants respectfully submit that the specification contains a sufficient written description of the claimed variants to fulfill the requirements of 35 U.S.C. 112. Reconsideration and withdrawal of the rejection are therefore respectfully requested. No new matter was added.

III: **The Rejection of Claims 25-30, 50, 57 and 59-66 under 35 U.S.C. § 112, first paragraph, (Written Description)**

Claims 25 and 59 are currently amended. Reconsideration is urged. Moreover, Applicants note the following:

The written description requirement of the Patent Code is fulfilled when the patent specification describes the claimed invention in sufficient detail such that one skilled in the art can reasonably conclude that the inventor had possession of the claimed invention. *See Vas-Cath, Inc. v. Mahurkar*, 19 USPQ2d 1111, 1116 (Fed. Cir. 1991). The written description as filed is presumed to be adequate, unless or until sufficient evidence or reasoning to the contrary has been presented by the examiner to rebut the presumption. *See In re Marzocchi*, 169 USPQ 367 (CCPA 1971). Under this standard, the Examiner's conclusion that the specification fails to distinguish between naturally occurring and non-naturally occurring is plainly incorrect. The specification discloses, and one skilled in the art would clearly recognize, that the scope of the present invention includes non-naturally occurring alpha-amylases, or variants that are purified. For example, examples have been included which show, *inter alia*, the materials and methods, on page 31 which refers specifically to AA560 of SEQ ID NO: 12 as disclosed in WO 00/60060 and available from Novozymes; Plasmids for use in accordance with the present disclosure are also shown and described on page 31. Methods which include, *inter alia*, model building, vector construction, various filter assays, methods of obtaining the regions of interest, fermentation and *purification* of alpha amylase variants (emphasis added), stability determination, assays for alpha-amylase activity, and general methods of random mutagenesis are described on pages 31-38. Further, Example 3 shows homology building of AA560 tertiary structure (See page 40). Example 4 shows method of extracting important regions for identifying AA560 alpha-amylase variants with altered properties (See page 41). Example 5 shows construction by localized random doped mutagenesis of AA560 alpha amylase variants having increased solubility in comparison to the parent enzyme (See page 42-43). Example 6 specifically shows the construction of variants of AA560 shown in SEQ ID NO: 12. Example 6 specifically states that the construction of other variants of the invention were carried out in a similar manner.

Given the detailed disclosure on how to construct the variants, including but not limited to fermentation and purification of alpha-amylase variants in accordance with the present disclosure an artisan would know whether recombinant means were used to obtain the variants in accordance with the present disclosure. As Applicants included the terms "purified", "variants" (with respect to claim 25), and "purified non-naturally occurring, modified parent alpha-amylase" (with respect to

claim 59)-- non-natural embodiments are clearly envisioned by an artisan once apprised of Applicants' invention.

Notwithstanding the above, the Examiner has not provided sufficient evidence or reasoning to rebut that the specification provides an adequate written description for purified variant(s) or purified non-naturally occurring, modified parent alpha-amylase as claimed.

Therefore, Applicants respectfully submit that the specification contains a sufficient written description of the claimed variants and non-naturally occurring alpha-amylases to fulfill the requirements of 35 U.S.C. 112. Reconsideration and withdrawal of the rejection are therefore respectfully requested.

IV: The Rejection of Claims 50, 57, 65 and 66 Under 35 U.S.C. § 112, second paragraph

Claims 50 and 65 are canceled. Claims 57 and 66 are currently amended. Reconsideration is urged.

V. The Rejection of Claims 25, 27-28, 30, 59, 61, 62 and 64 under 35 U.S.C. 102(b)

Claims 25, 27-28, 30, 59, 61, 62 and 64 are rejected under 35 U.S.C. 102(b) as being anticipated by U.S. patent No. 5,824,531 (Hereinafter referred to simply as "Outtrup A" and U.S. patent No. 5,856,164 (hereinafter referred to simply as "Outtrup B").

Independent claims 25 and 59 are currently amended. Accordingly, Applicants have been fully responsive to the Examiner's rejection and reconsideration is urged. Support for the term purified can be found, *e.g.*, on page 34.

Applicants further note that the alpha-amylase of Outtrup et al. does not read on the claims as the claims are directed to a "purified" "variant" alpha-amylases having a "substitution" at an amino acid position 118, 320 and/or 458 in SEQ ID NO:12. The use of the terms "purified" "variant" and "substitution" distinguishes the claimed alpha-amylases from the wild-type enzyme of Outtrup et al. which is not a "purified variant", especially one having a "substitution" at the recited position(s). It also clearly does not have a substitution of "R118K", "R320K" or "R458K."

As noted above in section III, given the detailed disclosure on how to construct the variants, one of ordinary skill in the art would know whether recombinant means were used to obtain the purified variants in accordance with the present disclosure.

Applicants respectfully submit that the specification clearly uses the term "variant" to refer to "man made" variants and not variants made in nature. This is illustrated, *e.g.*, in the specification at page 4, lines 9-14, page 13, lines 6-19, and page 24, lines 11-15, which clearly illustrate that the

term variant means non-naturally occurring. In particular, the specification discloses that the variants have changes to the naturally-occurring amino acid, and therefore, are not found in nature.

In addition to the term variant, independent claims 25 and 59 also employ the term "purified" which together with the terms "variant" and "substitution" clearly would be envisioned by an artisan once apprised of Applicants' invention as non-natural embodiments. Clearly, natural variants are not encompassed by claims 59-66 which are directed to alpha-amylase(s) which are non-naturally occurring or modified and in which the modification is not naturally present in the parent alpha-amylase.

Accordingly, the claims are not anticipated by Outtrup *et al* because the claims do not encompass wild-type enzymes. Moreover, a skilled artisan would understand that the claims encompass non-naturally occurring alpha-amylases and do not encompass the naturally occurring alpha-amylase of Outtrup et al.

For the foregoing reasons, Applicants submit that the claims overcome this rejection under 35 U.S.C. 102. Applicants respectfully request reconsideration and withdrawal of the rejection.

VI. The Rejection of Claims 25, 27-28, 30, 59, 61, 62 and 64 under 35 U.S.C. 102(e)

Claims 25, 27-28, 30, 59, 61, 62 and 64 are rejected under 35 U.S.C. 102(e) as anticipated by US Patent Nos. 6,093,562, 6,187,576, 6,197,565, 6,204,232, 6,287,826, 6,297,038, 6,361,989, 6,486,113, 6,528,298, 6,673,589, 6,867,031, and 6,887,986.

Initially, independent claims 25 and 59 have been amended to refer to 95% homology. Accordingly, Applicants have been fully responsive to the Examiner. Reconsideration of amended claims 25 and 59 is urged.

Further, for the same reasons discussed above, the alpha-amylases of US Patent Nos. 6,093,562, 6,187,576, 6,197,565, 6,204,232, 6,287,826, 6,297,038, 6,361,989, 6,486,113, 6,528,298, 6,673,589, 6,867,031 and 6,887,986 also do not read on the claims as they do not disclose purified variant alpha-amylases having a substitution of a lysine at a position selected from the group consisting of 118, 320 and 458 (claims 25-20 and 50) or the isolated non-naturally occurring, modified parent alpha amylases (claims 59-66).

For the foregoing reasons, Applicants submit that the claims overcome this rejection under 35 U.S.C. 102. Applicants respectfully request reconsideration and withdrawal of the rejection.

VII. Double Patenting

Claims 25, 27-28, 30, 59, 61, 62 and 64 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over US Patent Nos. 6,093,526,

6,187,576, 6,197,565, 6,204,232, 6,297,038 and 6,673,589. This rejection is respectfully traversed.

Claims 25 and 59 are currently amended and include, *inter alia*, 95% homology. The cited art does not show this feature or make these claims obvious. Reconsideration is urged.

For the foregoing reasons, Applicants submit that the claims overcome the obviousness type double patenting rejection. Applicants respectfully request reconsideration and withdrawal of the rejection.

VIII: New Claims:

New Claim 67 is added. Should any additional fees be due, the U.S. Patent and Trademark Office if authorized to charge any such fee to the deposit account of Novozymes North America, Inc, *i.e.*, deposit account no. 50-1701.

IX. Conclusion

In view of the above, it is respectfully submitted that all claims are in condition for allowance. Early action to that end is respectfully requested. The Examiner is hereby invited to contact the undersigned by telephone if there are any questions concerning this amendment or application.

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